Remarks

I. Applicants' Invention and Preliminary Comments

Applicants' invention relates to methods of use of compounds that possess one or more ionic and hydrophobic chemical moieties spatially located so at to mimic the spatial location of at least an ionic or hydrophobic amino acid residue of insulin. That is, the compounds of the present invention mimic the three-dimensional structure of amino acids of insulin and are designed to interact with the insulin binding site of the insulin receptor.

Claim 1 is amended herein to specify that hyperglycemia, including hyperglycemia associated with diabetes, is treated by the claimed method. This amendment finds support in the specification at, for example, page 9, line 28 through page 12, line 3 where hyperglycemia associated with diabetes is discussed. The amendment does not include new matter.

II. The Outstanding Rejections

Claims 1-10, 16, 17 and 20-25 stand rejected under 35 U.S.C. §112, second paragraph, for reciting Alzheimer's disease as an insulin-related ailment. Claim 17 is also rejected for reciting a method for determining both whether a compound is an agonist or whether a compound is an antagonist.

Claims 1-10, 16 and 17 stand rejected under 35 U.S.C. §102 over Sportsman et al. U.S. Patents 5,851,988 ("Sportsman I") and 6,329,431 ("Sportsman II").

III. Reasons for Patentability

A. The Rejections under 35 U.S.C. §112 May Be Withdrawn

In the Action, the examiner took the position that the specification on page 26 does not definitely identify Alzheimer's disease as a insulin-related ailment and further that Alzheimer's disease is not recognized in the art as an insulin-related ailment. In response, Applicants submit that the paragraph at page 26, lines 6-12 of the present specification does identify Alzheimer's disease as an insulin-related ailment and that paragraph renders the claim definite. The reference to "[o]ther ailments" in the paragraph is a reference to other insulin-related ailments and Alzheimer's disease is clearly mentioned as one of those other ailments. The examiner is respectfully requested to reconsider the paragraph as a whole.

The examiner also took the position that claim 17 should be amended to refer to determining whether a compound is an agonist only or an antagonist only. In response,

Applicants note that when a person carries out the method of claim 17, the person will see either an increase in biological activity or a decrease in biological activity. If there is an increase in biological activity it indicates that the compound of interest is a agonist, while if there is a decrease in biological activity it indicates that the compound is an antagonist. Thus, due to the possible effects of the claimed method on biological activity, it is logical that the claim recites identification of both agonists and antagonists.

The rejections under Section 112, second paragraph, may therefore properly be withdrawn.

B. The Rejections under 35 U.S.C. §102 over Sportsman I and II May Be Withdrawn.

Claims 1-10, 16 and 17 are not anticipated by Sportsman I or II because neither document teaches compounds that mimic insulin (as is required by the present claims) and that are intended to interact with the insulin binding site of the insulin receptor. Instead, the Sportsman documents teach "insulin agonist" compounds that interact with the kinase portion of the insulin receptor (*see* Sportsman I, column 8, lines 27-29 and Sportsman II, column 6, lines 43-45) and teach that stimulation of receptor activity by the compounds is independent of the peptide hormone [insulin] binding site (*see* Sportsman I, column 1, line 66 through column 2, line 2 and Sportsman II, column 2, lines 3-6). Sportsman I and II use the phrase "insulin agonist" in a manner that does not imply that the compounds of the Sportsman documents interact with the insulin binding site of the insulin receptor. Rather, the term is used to describe the broad pharmacological properties of the compounds.

The compounds disclosed in Sportsman I and II may have both ionic and hydrophobic moieties, but those moieties are not spatially located to mimic the spatial location of amino acids of insulin as is required by the present claims. This difference is responsible for the Sportsman compounds binding to the kinase portion of the insulin receptor (*see again*, Sportsman I, column 8, lines 27-29 and Sportsman II, column 6, lines 43-45) while the compounds of the present claims, by virtue of having ionic and hydrophobic moeties spatially located so as to mimic the spatial location of amino acid residues of insulin, are designed to bind to the insulin binding site of the insulin receptor. As is shown in the examples in the present application, experimental data suggests that the compounds of the claims compete directly with insulin for binding to the insulin binding site of the receptor.

Moreover, because the Sportsman compounds and the compounds of the present invention are designed to bind to the insulin receptor at different functional sites, the effect of the compounds on activation of the receptor is different. The Sportsman patents themselves say that the Sportsman compounds do not effect activation of the receptor by a mechanism similar to that exhibited by insulin (*see*, for example, the second paragraph of the "Modes of Carrying Out the Invention" of the Sportsman documents). Referring to Figure 1 of both Sportsman I and II, the Sportsman compounds lead directly to activation of the kinase activity associated with the "catalytic domain" without interacting with the "ligand binding domain." In direct contrast, the compounds of the present invention are designed to interact with the ligand binding domain.

Accordingly, claims 1-10, 16 and 17 are novel over Sportsman I and II and may be allowed.

Conclusion

In view of the foregoing remarks, Applicants respectfully request early notice of allowance of all the pending claims. Should the examiner wish to discuss any issues of form or substance in order to expedite allowance of the pending application, she is invited to contact the undersigned agent at the number indicated below.

Respectfully Submitted,

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